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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/514,113	02/28/2000	Frank B. Dean	MSI 100	9257

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EXAMINER
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SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

9M

<b>Office Action Summary</b>	<b>Application No.</b> 09/514,113	<b>Applicant(s)</b> DEAN ET AL.	
	<b>Examiner</b> Bradley L. Sisson	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 February 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-19,21-23,27,31-45 and 77-80 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19,21-23,27,31-45 and 77-80 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                            | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### ***Prosecution Reopened***

1. In view of the newly discovered prior art (US Patent 6,265,559 B1 (Gildea et al.)) filed on 12 May 2000, with a priority date of 7 June 1995, PROSECUTION IS HEREBY REOPENED. News grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) File a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) Request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

### ***Specification***

2. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states at page 25: "Publications cited herein and the material for which they are cited are specifically incorporated by reference." Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be

Art Unit: 1634

found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USPQ 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6<sup>th</sup> Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1634

4. Claims 1-19, 21-23, 27, 31-45, and 77-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 1, 21-23, 44, 45, 77, 79, and 80 provides for the use of template deficient oligonucleotides, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claims 2-19, 27, 31-45, and 78, which depend from independent claims 1, 23, 77, 79 and 80, fail to overcome this issue and are similarly rejected.

Claims 1-19, 21-23, 27, 31-45 and 77-80 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### ***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1, 5, 8-10, 19, 22, and 77 are rejected under 35 U.S.C. 102(a), (e) as being anticipated by Wallace (US Patent 6,027,923).

9. Wallace, columns 9 and 10, disclose the use of primers that contain a non-replicable element wherein said primers are used in a nucleic acid amplification reaction. Figures 3-5 show that the modified nucleotide is located several bases upstream, or 5', to the template capable portion of the primer.

10. Wallace, column 9, third and fourth paragraphs, disclose the use of abasic nucleotides in primer used in an amplification reaction. The teaching of "primers that contain non-replicable and/or cleavable elements" (column 9, lines 18-19) has been interpreted as there being a plurality of such nucleotides in a primer. Also, column 9, lines 32-33, teaches the presence of "a residue" in a primer. Accordingly, Wallace is considered to teach the use of one or more such abasic nucleotides.

### ***Claim Rejections - 35 USC §102/103***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1634

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-19, 21-23, 27, 31-45 and 77-80 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Van Ness et al.

16. Page 6, bridging to page 7 of the specification reads in part:

Art Unit: 1634

Template-deficient nucleotides are selected from the group consisting of modified nucleotides, derivatized nucleotides, ribonucleotides, and nucleotide analogs. Preferred template-deficient nucleotides are modified nucleotides. Preferred modified nucleotides are abasic nucleotides. Template-deficient nucleotides include abasic nucleotides, nucleotides with an inverted base, fluoro substituted nucleotides, alkyl substituted nucleotides, nucleotides with phenyl substituted ethers, nucleotides with substituted thioethers, nucleotides with substituted esters,  $\alpha$ -nucleotides, 2', 3'-dideoxy nucleotides, ribonucleotides, nucleotides derivatized with biotin, nucleotides derivatized with amine, nucleotides derivatized with Hex, nucleotides derivatized with Tet, nucleotides derivatized with Fam, nucleotides derivatized with fluorescein, nucleotides derivatized with rhodamine, nucleotides derivatized with alkaline phosphatase, nucleotides derivatized with horseradish peroxidase, nucleotides derivatized with spacers, nucleotides derivatized with cholesteryl, nucleotides derivatized with DNP-TEG, nucleotides derivatized with psoralen cross-linkers, nucleotides derivatized with intercalating agents, and nucleotides derivatized with PNA conjugates.

17. In view of the definition of "template-deficient nucleotides" that has been provided, the claims have been interpreted to encompass the use of primers that comprise abasic nucleotides as well as being labeled or stained with an intercalating agent.

18. Van Ness et al., at columns 82-85 disclose performing amplification reactions where one or more abasic nucleotides are incorporated into a primer. As seen in TABLE 14, at least one of the primers contained modified nucleotides located at the 5' terminus, other primers contained modified nucleotides within three nucleotides of the 5' terminus. Column 84 depicts several of the primer sequences. As seen therein, different modified nucleotides were incorporated in the primers.



Art Unit: 1634

## Example 6

## Introduction of an Abasic Site into an Oligonucleotide Increases the HCT of the Oligonucleotide and Improves Priming Specificity

As demonstrated above (Example 3), an abasic site or mismatched site introduced into an oligonucleotide primer decreases the  $T_m$  and HCT of the respective derived primer compared to a perfectly based pair "sister" primer. Abasic sites in polynucleotides or oligonucleotides can be introduced by the chemical or enzymatic hydrolysis of the glycosidic bond. The resulting structure is apurinic or apyrimidinic which lacks the coding information and fails to base pair. The CE phosphoramidite of the tetrahydrofuran derivative is commercially available (dSPACER, Glenn Research, Sterling, Va.) as well as other spacer phosphoramidites (Glenn Research, Sterling, Va.). In addition, abasic sites can be introduced by phosphoramidite synthesis.

The effect of abasic substitutions on the HCT of a set of oligonucleotides is shown in Table 12.

TABLE 12

Buffer Type	Oligo Type	HCT*	$T_m$ *	Stringency Factor
1X PCR buffer	normal	24	65	
1X PCR buffer	deoxynebularine	22	64	
0.5 M DMCHAA	normal	18	37	
0.5 M DMCHAA	deoxynebularine	14	32	
1X PCR buffer	normal	18		
1X PCR buffer	abasic (dSPACER)	12		
1X PCR buffer	abasic (C3 spacer)	12		
0.5 M TMAHCA	normal	14		
0.5 M TMAHCA	abasic (dSPACER)	8		
0.5 M TMAHCA	abasic (C3 spacer)	8		
2.0 M LiTCA	normal	12.5	44.5	4.97
2.0 M LiTCA	abasic	10	39	6.37
	(dSPACER)deoxynebularine			
2.0 M LiTCA	abasic (dSPACER)	10	39	6.37
2.0 M LiTCA	abasic (C3 spacer)	10	39	6.25
3.0 M GuSCN	normal	16	35.5	3.85
3.0 M GuSCN	deoxynebularine	12.5	32	5.24

\* = °C.

Art Unit: 1634

Column 84, states in part:

40 Two regions in the bacteriophage lambda DNA sequence  
(GenBank Accession #J02459) are chosen as the priming  
sites for amplification. The 5' primer has a stable GC-rich 3'  
end; the 3' primer is chosen so that a 381 bp product will  
result from the amplification. The primers used in this  
45 example are as follows:  
Forward (5') primers:  
H17: 5'-GAACGAAAACCCCCCGC-3' (SEQ ID NO: 23)  
H14: 5'-CTTCGAAAACCCCCCGC-3' (SEQ ID NO: 24)  
H11: 5'-CTTGCTAAACCCCCCGC-3' (SEQ ID NO: 25)  
50 AB1: 5'-GAACGA(dS)AACCCC(dS)CGC-3' (SEQ ID NO:  
26)  
AB2: 5'-GAACGA(dS)AACCCC(dS)CCGC-3' (SEQ ID NO:  
27)  
AB3: 5'-GAACGA(dS)AACCCCCCG(dS)C-3' (SEQ ID  
55 NO: 28)  
DN1: 5'-GAACGA(dS)AACCCC(dN)CGC-3' (SEQ ID  
NO: 26)  
DN2: 5'-GAACGA(dNAACCCC(dN)CCGC-3' (SEQ ID NO:  
27)  
60 DN3: 5'-GAACGA(dN)AACCCCCCG(dN)C-3' (SEQ ID  
NO: 28)  
DN4: 5'-GAACG(dN)AAACCC(dN)CCGC-3' (SEQ ID  
NO: 29)  
DN5: 5'-GAACG(dN)AAACC(dN)CCCGC-3' (SEQ ID  
65 NO: 30)  
DN6: 5'-CTTCGAAAACCCC(dN)CCGC-3' (SEQ ID NO:  
31)

Continuing to Column 85:

Art Unit: 1634

US 6,361,

85

Reverse (3') primer:

reverse: 5'-GATCGCCCCCAAAACACATA-3' (SEQ ID

NO: 32)

(dS) represents "dSPACER" residue and (dN) represents deoxyNebularine residue.

The forward primers are designed with their 5' ends variably mismatched to the target DNA. The H17 primer is a perfect match to the intended target, whereas the primer H14 is complementary only for the 14 nucleotides at the 3' end (the 3 nucleotides at the 5' end are mismatched). All of the primer pairs are used in separate amplification reactions, and the annealing temperature is varied from 25° C. to 65° C. A set of typical results are presented in Table 14, wherein "dNeb." stands for deoxyNebularine. Similar results are obtained for both Taq and Pfu polymerases.

TABLE 14

Primer Name	Number mismatches @ position in primer	Substitutions	Temp. Range (° C.) that amplifications observed	
H17	none	none	25 ----> 65	
H14	3 @ 5'	none	25 ----> 65	
H12	6 @ 5'	none	25 ----> 50	
AB1	2, @ 7, 14	dSpacer™	no amplification	
AB2	2, @ 7, 13	dSpacer™	no amplification	
AB3	2, @ 7, 16	dSpacer™	no amplification	
DN1	2, @ 7, 14	dNeb.	25 ----> 35	
DN2	2, @ 7, 13	dNeb.	25 ----> 35	
DN3	2, @ 7, 16	dNeb.	25 ----> 30	
DN4	2, @ 6, 13	dNeb.	25 ----> 35	
DN5	2, @ 6, 12	dNeb.	25 ----> 35	
DN6	2, 3 @ 5', 13	dNeb.	25 ----> 30	

These results indicate that the dSpacer substitution prevents the Taq or Pfu DNA polymerase from "reading through" the abasic site. That is, when the polymerase encounters an abasic residue, chain extension is terminated. Therefore, the priming site is not conserved during the second strand synthesis, and amplification of the target nucleic acid is not achieved. However, the polymerases can read through deoxyNebularine residues present in the oligonucleotide primers. Most likely, but not verified, deoxythymidine is inserted as the complementary base to deoxyNebularine. However, the temperature range over which amplification is achieved is reduced compared to the temperature range for amplification using the H17 primer (from 25° C.-65° C. down to 25° C. to approximately 35° C.). It is therefore apparent that the deoxyNebularine substituted primers can substantially increase the specificity of the PCR reaction. Priming was improved which led to the amplification of a specific amplicon.

In view of the above showing, and in the absence of convincing evidence to the contrary, the disclosure of Van Ness et al., is considered to meet the limitations of claims 1-19, 21-23, 27, 31-45 and 77-80.

***Claim Rejections - 35 USC § 103***

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1634

22. Claims 1-19, 21-23, 27, 31-45 and 77-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,361,940 B1 (Van Ness et al.) in view of US Patent 6,265,559 B1 (Gildea et al.) or US Patent 6,316,230 B1 (Egholm et al.).

23. See above for the basis of the rejection as it pertains to the disclosure of Van Ness et al. Van Ness et al., do not disclose chimeric primers/oligonucleotides that comprise PNA conjugates.

24. Gildea et al., column 18, disclose synthesis of chimeric oligonucleotides that comprise a PNA portion as well as DNA or RNA portions. Columns 35-36 disclose further comprising linkers as well as detectable moieties. And column 41 discloses using these chimeras in amplification reactions such as PCR.

25. Egholm et al., disclose performing PCR, RT-PCR using chimeric primers that comprise PNA conjugates.

26. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the procedure of Van Ness et al., such that other modified nucleotides were incorporated into the primers from a taught by both Gildea et al., and Egholm et al., chimeric primers had already been developed and disclosed as being useful in amplification reactions five years prior to the filing of the subject application (Gildea et al.).

While applicant has claims drawn to specific combinations of modified nucleotides, such limitations are considered to be the result of routine optimization and do not rise to the level of a patentable difference over the prior art. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this

Art Unit: 1634

position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233

(CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. *In re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; *In re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. *In re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; *In re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. *In re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; *In re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; *In re Irmischer*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

27. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-19, 21-23, 27, 31-45 and 77-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,361,940 B1 (Van Ness et al.) in view of US Patent 6,265,559 B1 (Gildea et al.) or US Patent 6,316,230 B1 (Egholm et al.).

### ***Conclusion***

28. To the extent that applicant has presented argument in the Appeal Brief, the traversal raised therein is considered to effectively repeat argument previously presented, and which was responded to in the Final Office Action of 16 July 2003 and Advisory Action of 31 October 2003.

Art Unit: 1634

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

31. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson  
Primary Examiner  
Art Unit 1634

BLS

11 July 2004